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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,782	02/06/2002	Gary L. Griffiths	018733-1089	5555

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,782	GRIFFITHS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 20-48* is/are pending in the application.

4a) Of the above claim(s) *20-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of the application has changed. This case has now been transferred as of July 31, 2006. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Brandon Fetterolf, Group Art Unit 1642.

Election/Restrictions

The Election filed on 2/13/2006 in response to the Restriction Requirement of 1/11/2006 has been entered. Applicant's election of Group I, claims 1-14 and 48, as specifically drawn to a method of increasing the target-specific toxicity of a drug has been acknowledged.

Applicant's election with traverse of Group I, claims 1-14 and 48, is acknowledged. The traversal is on the grounds that the claims of Group II have already been searched and examined and including these claims will not pose a burden on the Examiner. Applicants note that claims 20-47 were already deemed allowable (subject to filing a terminal disclaimer) and therefore, query as to why a restriction requirement is imposed here. In addition, Applicants contend that the office action indicates that examination on the merits has been reopened on the basis of specific prior art. As such, Applicants assert that it would not impose a burden on the Examiner to apply this newly identified art to the claims of Group II.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants arguments pertaining to the search of all the claims in the previous office action, the instant Examiner can not comment on why a restriction was not made and all claims examined on the merits. However, the instant Examiner recognizes that the claims of an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § **> 802.01, § 806.06, and § 808.01<) or distinct (MPEP § 806.05 - § *> 806.05(j)<). In the instant case, the inventions are classified differently, necessitating different searches of the US Patents. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-14 and 20-48 are currently pending

Claims 20-47 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-14 and 48 are currently under consideration.

Species Election

Applicant's have elected the following species for initial examination on the merits:

-Pretargeting agent: the bispecific antibody hMN14 IgG x 734 Fab;

-Cytotoxic drug or prodrug: CPT-11

-Enzyme-combination of carboxylesterase and glucuronidase

-Clearing agent: Galactosylated version of anti-idiotype antibody, WI2, (Gal-WI2)

Upon further review and reconsideration, the Examiner has withdrawn the species requirement. As such all species will be examined on the merits.

Claim Objections

Claim 6 is objected to because of the following informalities: The terminology of claim 6 is confusing. It is suggested that claim 6 be amended to recite "The method of claim 5, further comprising pretargeting an esterase to said target site that cleaves CPT-11 to SN-38.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-14 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are inclusive of a method for increasing the target-specific toxicity of a drug,

comprising pretargeting an enzyme to a mammalian target site; and administering a cytotoxic drug known to act at the target site, or a prodrug form thereof which is converted to the drug in situ, which drug is also detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme and thus has enhanced cytotoxicity at the target site. Thus, the claims are drawn to a genus of cytotoxic drugs which is detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes. However, the written description in this case only sets forth a sub-genus of cytotoxic drugs, wherein the sub-genus are chemotherapeutic agents.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 8, 4th full paragraph) that the drug or prodrug must be soluble for the purposes of administration and transport to the target site and the drug must also be capable of being converted to a detoxified form, e.g., a glucoranide, sulfate or glycoside, but the mammalian body. The specification further teaches (page 9, 3rd full paragraph) that the conversion of certain toxic substances such as aromatic or alicyclic alcohols, thiols, phenols and amines to glucuronides in the liver is the body's method of detoxifying them and making them more easily excreted in the urine. For examples, the specification teaches (page 9, beginning at the 3rd full paragraph) that certain antitumor drugs such as epirubicin, a 4-epimer of doxorubicin, 5-fluorouracil, the prodrug CPT-11, etoposide can be used in the instant invention. Thus, while the specification reasonably conveys a representative number of anti-tumor agents, the specification does not appear to commensurate in scope of the instant claims, i.e., any and/or all cytotoxic drugs. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119

F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of drugs that encompass the genus of cytotoxic drugs which is detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes nor does it provide a description of structural features that are common to the genus. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of cytotoxic drugs, and therefore conception is not achieved until reduction to

practice has occurred, regardless of the complexity or simplicity of the method of isolation. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species) Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a sub-genus of cytotoxic drugs, wherein the sub-genus encompasses chemotherapeutic agents, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 11 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (WO 91/08770, 1991).

Hansen teaches a method for increasing the target-specific toxicity of a drug, comprising pretargeting an enzyme to a human target cell; and administering a cytotoxic drug or a prodrug form thereof known to act at the target site, wherein the enzyme is capable of forming the active

therapeutic agent (page 4, line 13 to page 5, line 2 and page 46, lines 4-5). Specifically, the WO document teaches that the enzyme is pretargeted to a target cell using an antibody-enzyme conjugate (page 5, lines 14-15). With regards to the enzyme, the WO document teaches that suitable enzymes include, but are not limited to, glucuronidase, beta-glucosidase, beta-lactamase, cellulose, dextranase, fructose, aminopeptidase and lysozyme (page 9, lines 22-31). With regards to the antibody, the WO document teaches that the antibodies include, but are not limited to, monoclonal antibodies, antibodies having dual or multiple antigen or epitope specificity or fragments thereof including hybrid fragments (page 6, lines 22-30 and page 7, lines 11-22). Regarding the drug, the WO document teaches that the one type of anti-tumor drug that can be converted to a substrate for glucurodinase is an anthracycline glycoside referred to as epirubicin (page 14, lines 25-35). In addition, Handen teaches that the clearance of the antibody-enzyme conjugate and/or the substrate-enzyme conjugate can be accelerated by using a second antibody complex which recognizes the conjugate and enhances the rate of uptake by macrophages (page 25, lines 20-33). Thus, while Hansen does not explicitly teach that the epirubicin is detoxified to form an intermediate of lower toxicity, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme, the claimed limitation does not appear to result in a manipulative difference in the method steps when compared to the prior art disclosure because the specification teaches (page 9, 3rd full paragraph) that drugs such as epirubicin which are detoxified in the liver to glucuronides such as epirubicin are suitable candidates for the site specific enhancement methods of the present invention. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). In the instant case, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. (WO 91/08770, 1991) in view of Griffiths et al (WO 96/40245, 1996).

Hansen teaches, as applied to claims 1-4, 11 and 48 above, a method for increasing the target-specific toxicity of a drug, comprising pretargeting an enzyme to a human target cell; and administering a cytotoxic drug or a prodrug form thereof known to act at the target site, wherein the enzyme is capable of forming the active therapeutic agent (page 4, line 13 to page 5, line 2 and page 46, lines 4-5). Specifically, the WO document teaches that the enzyme is pretargeted to a target cell using an antibody-enzyme conjugate (page 5, lines 14-15). With regards to the enzyme, the WO document teaches that suitable enzymes include, but are not limited to, glucuronidase, beta-glucosidase, beta-lactamase, cellulose, dextranase, fructose, aminopeptidase and lysozyme (page 9, lines 22-31). With regards to the antibody, the WO document teaches that the antibodies include, but are not limited to, monoclonal antibodies, antibodies having dual or multiple antigen or epitope specifities or fragments thereof including hybrid fragments (page 6, lines 22-30 and page 7, lines 11-22). Moreover, the WO document teaches that bispecific antibodies can also be used as the antibody-enzyme conjugate, wherein the bispecific antibody contains at least one binding site specific to an antigen at the target site and at least one other binding site specific to the enzyme component of the antibody-enzyme conjugate, thereby obviating the need to covalently conjugate the enzyme to the antibody (page 8, lines 24-37). Regarding the drug, the WO document teaches that the one type of anti-tumor drug that can be converted to a substrate for glucurodinase is an anthracycline glycoside referred to as epirubicin (page 14, lines 25-35). In addition, Handen teaches

that the clearance of the antibody-enzyme conjugate and/or the substrate-enzyme conjugate can be accelerate by using a second antibody complex which recognizes the conjugate and enhances the rate of uptake by macrophages (page 25, lines 20-33). Thus, while Hansen does not explicitly teach that the epirubicin is detoxified to form an intermediate of lower toxicity, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme, the claimed limitation does not appear to result in a manipulative difference in the method steps when compared to the prior art disclosure because the specification teaches (page 9, 3rd full paragraph) that drugs such as epirubicin which are detoxified in the liver to glucuronides such as epirubicin are suitable candidates for the site specific enhancement methods of the present invention. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). In the instant case, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Hansen does not explicity teach that the antibody used during the clearing step is an anti-idiotypic antibody, wherein the anti-idiotypic antibody is specific for the paratope of the monoclonal antibody conjugate to the enzyme.

Griffiths et al. teach an improvement in *in vivo* pretargeting methods, wherein the improvement involves the administration of a clearing agent that binds to the primary binding site of the primary targeting species, whereby substantially only non-localized primary targeting species are cleared and targeted primary targeting species are not removed from the target site (page 6, lines 7-35). For example, the WO document teaches that when the primary targeting species is an antibody, the clearing agent comprises an antibody which recognizes the antigen binding region (paratope) of the targeting antibody, i.e., the clearing agent comprises an anti-idiotypic second antibody (page 9, lines 1-12 and page 10, line 38 to page 11, line 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method taught by Hansen with an anti-idiotypic antibody in view of Griffiths et al teachings of an improved method of in vivo pretargeting. One would have

been motivated to do so because of Griffiths et al. teach that anti-idiotypic antibodies allow for the selective removal of non-localized targeting species and not the removal of targeting species from the target site. Thus, one of ordinary skill in the art would have a reasonable expectation that by using an anti-idiotypic antibody in the clearance step taught by Hansen, one would achieve a method of improving pretargeting an enzyme-antibody conjugate for therapeutic purposes.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7 and 11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,074,405.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. The species method of treating diseased tissues in a patient comprising: A) administering to said patient a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate; (B) optionally, administering to said patient a clearing composition, and allowing said composition to clear non-localized antibodies or antibody fragments from circulation; (C) administering to said patient a first targetable conjugate which comprises a carrier portion and one or more conjugated enzymes, wherein said carrier portion comprises or

bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment; and (D) administering to said patient (1) a drug which is capable of being detoxified in said patient to form an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the targeted tissue claimed in the conflicting patent application appears to fall within the same scope of the genus method for increasing the target-specific toxicity of a drug, comprising pretargeting an enzyme to a mammalian target site; and administering a cytotoxic drug known to act at the target site, or a prodrug form thereof which is converted to the drug in situ, which drug is also detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme and thus has enhanced cytotoxicity at the target site claimed in the application under examination.

Claims 1, 4-5, 7 and 11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-5 of U.S. Patent No. 7,074,405.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. The species method of treating or identifying diseased tissues in a subject, comprising: (A) administering to said subject a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate comprising at least two HSG haptens, wherein said at least one other arm that specifically binds a targetable conjugate comprising at least two HSG haptens comprises the Fv of mAb 679; (B) optionally, administering to said subject a clearing composition, and allowing said composition to clear non-localized antibodies or antibody fragments from circulation; (C) administering to said subject a targetable conjugate which comprises a carrier portion which comprises or bears at least two HSG haptens and may comprise a diagnostic or therapeutic cation, and/or one or more chelated or chemically bound therapeutic or diagnostic agents, or enzymes; and (D) when said targetable conjugate comprises an enzyme, further administering to said subject 1) a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site; or 2) a drug which is capable of being detoxified in said subject to form an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site,

or 3) a prodrug which is activated in said subject through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site appears to fall within the same scope of the genus method for increasing the target-specific toxicity of a drug, comprising pretargeting an enzyme to a mammalian target site; and administering a cytotoxic drug known to act at the target site, or a prodrug form thereof which is converted to the drug in situ, which drug is also detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme and thus has enhanced cytotoxicity at the target site claimed in the application under examination.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER